Protocol Synopsis

PREVENT-PAS	
Objective(s)	The WATCHMAN Post Approval Study is designed to assess long term safety and effectiveness outcomes associated with the use and implantation of the WATCHMAN Left Atrial Appendage (LAA) Closure Technology in a routine clinical setting.
Intended Use	The WATCHMAN LAAC Device is a percutaneous, transcatheter closure device intended for non-surgical closure of the left atrial appendage. In considering the use of the WATCHMAN LAAC Device, the benefits and risks of the device and the rationale for an alternative to chronic warfarin therapy should be taken into account.
Test Device	WATCHMAN LAA Closure Technology
Device Sizes	21mm, 24mm, 27mm, 30mm, 33mm
Study Design	This is a non-randomized study that will prospectively enroll subjects newly implanted with the WATCHMAN device and retrospectively enroll subjects who were previously implanted with the WATCHMAN device in the Continued Access to PREVAIL (CAP2) clinical study (IDE G020312).
Planned Number of Subjects	Up to 1579 total subjects • 1000 prospective patients • Up to 579 retrospective (number of patients enrolled in CAP2)
Planned Number of Centers	Up to 100 sites located in the United States
1st Primary Endpoint	The occurrence of stroke (including ischemic and/or hemorrhagic), cardiovascular death (cardiovascular and/or unexplained cause) and systemic embolism at 24 months.
2nd Primary Endpoint	The occurrence (excluding the first 7 days post implant) of ischemic stroke or systemic embolism (thrombolic events) at 24 months.
3rd Primary Endpoint	The occurrence of one of the following events between the time of implant and within 7 days of the procedure or by hospital discharge, whichever is later: all-cause death, ischemic stroke, systemic embolism, or device or procedure related events requiring open cardiac surgery or major endovascular intervention such as pseudoaneurysm repair, AV fistula repair, or other major endovascular repair. Percutaneous catheter drainage of pericardial effusions, snaring of an embolized device, thrombin injection to treat femoral pseudoaneurysm and nonsurgical treatments of access site complications were excluded from this endpoint.

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Study Success Criteria	Study success will be declared on the basis of the three primary endpoints; that is, each must be met in order to declare success.
Method of Assigning Patients to Treatment	All subjects will be assigned the same treatment, as this is a single-arm study.
Follow-up Schedule	Subjects will be followed at intervals of 45 days, 12 months, and annually thereafter through 5 years post implant for assessment of adverse events.
Study Duration	Subjects will be followed through 5 years post implant. It is anticipated that the enrollment period will occur over a period of two years.
Required Medication Therapy	Warfarin, aspirin, clopidogrel, ticlopidine, prasugrel, heparin, antibiotics, as applicable and outlined within the protocol
Key Inclusion Criteria	Patients who meet all of the following criteria may be given consideration for inclusion in this clinical investigation, provided no exclusion criteria are met. 1. The patient is 18 years of age or older 2. The patient has non-valvular atrial fibrillation 3. The patient has a calculated CHA_2DS_2-VASc score of 2 or greater; 4. The patient is eligible for post implant warfarin therapy 5. Willing and capable of providing informed consent and participating in all testing/ visits associated with this clinical study at an approved clinical study center and at the intervals defined by this protocol
Key Exclusion Criteria	Patients who meet any of the following criteria will be excluded from this clinical study. 1. The patient has intracardiac thrombus or dense spontaneous echo contrast as visualized by peri-procedural TEE. 2. The patient has a history of atrial septal repair or has an ASD/PFO device 3. The patient's LAA anatomy will not accommodate a WATCHMAN device 4. The patient has any contraindications for other percutaneous catheterization interventions due to patient size (i.e. too small for TEE probe, catheter size, etc.) or condition (i.e. active infection, bleeding disorder, untreated ulcer, etc.) 5. The patient is contraindicated or allergic to aspirin and/or clopidogrel 6. The patient requires long term warfarin therapy for a condition other than atrial fibrillation. 7. The patient has a life expectancy of less than one year

<table>
<tr><th colspan="2">PREVENT-PAS</th></tr>
<tr><td>Statistical Methodology</td><td>
Hypotheses testing in this study will use standard statistical methodology.

The following patients will be excluded from all primary endpoint analyses:

Patients with prior stroke or TIA within the 90 days prior to enrollment.
Patients who experienced an MI within 90 days prior to enrollment.
Patients with symptomatic carotid disease (defined as >50% stenosis with symptoms of ipsilateral transient or visual TIA evidenced by amaurosis fugax, ipsilateral hemispheric TIAs or ipsilateral stroke).

<table>
<tr><th>Endpoint</th><th>Assessment period</th><th>Performance Goal</th><th>Test (α=5%)</th><th>Expected Attrition</th><th>Power[1]</th></tr>
<tr><td>1st Primary</td><td>0 to 2 years</td><td></td><td>Pointwise log-log upper confidence limit of Kaplan-Meier rate</td><td>20%</td><td>≥94%%</td></tr>
<tr><td>2nd Primary</td><td>0 to 2 years</td><td>5.7%</td><td>Pointwise log-log upper confidence limit of Kaplan-Meier rate</td><td>20%</td><td>≥92%</td></tr>
<tr><td>3rd Primary</td><td>7 days of hospital discharge, whichever is later</td><td>3.7%</td><td>One-sided exact test</td><td>0%</td><td>≥83%</td></tr>
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[1] Assumes 1579 patients will be available for the endpoint analysis at the beginning of the assessment period.
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Visit Schedule

Procedure/Assessment	Screening	Implant	45-Day (± 15 Days) Office Visit	1Year (± 60 Days) Office Visit	2 Year (± 60 Days) Office Visit	3-, 4- and 5-Years (± 60 Days) Telephone Interview
Informed consent	X					
Demographics and medical history	X					
Physical assessment including vital signs	X		X	X	X	
Transesophageal echocardiogram (TEE)	X	X	X	X		
Anticoagulant and antiplatelet medications	X		X	X	X	X
Modified Rankin Scale	X		X	X	X	X
Device and implant details		X				
Adverse event monitoring		X	X	X	X	X
Labs (eGFR and proteinuria)	X					